C2
cont.

(iii) forming a tablet by direct compaction of said mixture.

REMARKS

This is in response to the Final Office Action dated October 8, 2002. Claims 1-50 have been canceled, without prejudice. New claims 55-111 have been added. Reconsideration of the above identified application, in view of the above amendments and the following remarks, is respectfully requested.

Claim Objections

The allowability of claims 51-54, pursuant to a telephone conference on January 9, 2003 between Examiner Prior and Applicants' representative is noted. In the Office Action, the Examiner objected to claims 51-54 for depending from a rejected claim, and indicated that claims 51-54 would be allowable if rewritten in independent form. However, pending claim 51 was an independent claim and claims 52-54 dependent from claim 51. When this was brought to the Examiner's attention during the telephone conference, the Examiner indicated that he had intended to allow claims 51-54. Accordingly, it is understood that claims 51-54 are allowable.

Claim Rejections Under 35 U.S.C. §103: Obviousness

Claims 1-50 stand rejected as obvious over U.S. Patent 5,116,619 to Greco et al. ("the Greco patent"). The Examiner contends that the term "comprising" in independent claims 1, 2, 40 and 41 does not exclude mixing the micronized progesterone with ingredients other than

water, prior to drying, in the first step of the claims. The Examiner therefore concludes that the claims in their present form read on the method described in Example 2 of the Greco patent, which teaches mixing lactose and progesterone with starch prior to drying. The Examiner suggests amending the claims to clearly recite that no ingredients other than water are mixed with the micronized progesterone prior to drying the micronized progesterone for use in a direct compaction tabletting process.

By this Amendment, claims 1-50 have been canceled without prejudice and new claims 55-111 have been added. Support for the new claims are found in the original claims and in the specification in Example 1, page 9, Step 1. It is respectfully submitted that new independent claims 55-56, 98-99, and 109-111 address the Examiner's arguments and make it clear that the micronized progesterone is first mixed with water and *no other ingredients* (*i.e.*, excipients, diluents, etc.), and is then completely dried prior to further processing. It is only after the wetted micronized progesterone is dried that it is mixed with pharmaceutically acceptable excipients *in the absence of water* or other aqueous ingredients, and subjected to direct compaction into a tablet. The only aqueous mixture present in the process of the present invention is the combination of micronized progesterone and water. This mixture is dried before mixing with any excipients or diluents. Accordingly, the method defined by the present claims is not taught by the Greco patent. This is elaborated further below.

The Greco patent teaches in Example 2 that progesterone and lactose are mixed with a starch paste (*i.e.*, wet starch), to form a "damp mass" comprising progesterone, lactose and starch, which is then screened and dried. In Example 14, it is stated that progesterone, lactose

and starch in "powder form" are mixed with magnesium stearate. Although in Example 2, the Greco patent does not explicitly indicate whether the progesterone and lactose are wet or dry, it can be inferred that they are dry by the description of the ingredients in Example 1. Example 1 indicates that "The progesterone USP was a micronized powder obtained from the Upjohn Company" (column 6, lines 12-13); and "The lactose was obtained in powdered form from Sheffield Products..." (column 6, lines 34-35). Example 2 then describes mixing "the lactose and the progesterone". Accordingly, based on the ingredients disclosed in the patent, it is clear that the mixture of the lactose and progesterone in Example 2 of Greco, similar to the lactose, progesterone, starch and magnesium stearate in Example 14, is a dry mixture. None of the ingredients in Example 2 has been pre-wetted and/or pre-dried prior to mixing with any other ingredient.

The Examiner further contends that, in the previous amendment dated July 15, 2002, Applicants argued that Example 14 of the Greco patent teaches away from tablet formation using direct compression requiring the use of water. To the contrary, it was asserted that Example 14 of the Greco patent teaches away from forming a tablet using dry direct compression, *i.e.*, teaches away from the method of the present invention. See page 10 of the previous amendment. According to the Greco patent, the tablet prepared in the absence of aqueous media during the mixing and compacting processes, was inferior (column 10, lines 14-16).

The methods disclosed in the Greco patent do not suggest or disclose the method of the present claims. In the present invention, the micronized progesterone is wetted and dried prior to mixing with other ingredients (wet or dry). In contrast, in Example 2 of Greco, the micronized

progesterone is wetted in the presence of lactose and starch prior to drying. In Example 14 of Greco, none of the ingredients is wetted at any time prior to or during the tabletting process. In short, Greco does not suggest or disclose the method fo the present claims because Greco does not suggest mixing micronized progesterone and water in the absence of other ingredients.

To meet the burden of *prima facie* obviousness under 35 U.S.C. §103(a), the Examiner must establish that three criteria have been met. First, there must be a concrete suggestion or motivation to modify what is taught in a reference or to combine its teachings with other references. Second, there must have been a reasonable expectation that the modifications or combination would succeed. Finally, the combined or modified prior art must actually teach all of the claimed limitations. Both the motivation and the reasonable expectation of success must be found in the prior art and not in Applicants' disclosure. See, M.P.E.P §2143; citing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

It is therefore respectfully asserted that there is no teaching or suggestion in Greco to pre-wet only the micronized progesterone and to dry that composition prior to mixing with any other ingredients. The present inventors have unexpectedly discovered that direct compression using dry ingredients results in a superior tablet if the micronized progesterone is first pre-wetted and dried prior to mixing with the other excipients. Not only is the tablet superior for vaginal administration, as evidenced by the absence of residue buildup in the vaginas of women who are administered the tablet (see Declarations submitted with previous response), but dry direct compression is a faster, less expensive method of tablet formation. One of ordinary skill in the art would not have been motivated to modify the methods taught in the Greco patent and arrive

and the present invention since Greco teaches that (i) dry direct compression results in an inferior tablet (Example 14) and that (ii) a usable tablet is formed only when the micronized progesterone is mixed in aqueous media with other ingredients before drying (Example 2).

In view of the foregoing and the arguments presented above, withdrawal of this rejection is respectfully requested.

In view of the above amendments and remarks, the subsisting claims are believed to be in condition for allowance and such action is respectfully requested.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

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EXPRESS MAIL CERTIFICATE

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I hereby certify that, on the date indicated above, this paper or fee was deposited with the U.S. Postal Service & that it was addressed for delivery to the Assistant Commissioner for Patents, Washington, DC 20231 by "Express Mail Post Office to Addressee" service.

L. Stantini D. Stantini
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PATENT TRADEMARK OFFICE

Docket No: 4368/0J367

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Azariah JOSSIFOFF

Serial No.: 09/856,417 Art Unit: 1616

Confirmation No.: 7902

Filed: August 8, 2001 Examiner: A. Pryor

For: VAGINALLY ADMINISTRATABLE PROGESTERONE-CONTAINING TABLET AND METHOD FOR PRODUCING THE SAME

MARK-UP FOR AMENDMENT PURSUANT TO 37 C.F.R. §1.121

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

February 18, 2003

Sir:

IN THE SPECIFICATION

Please amend the title to read as follows:

VAGINALLY [ADMINISTRATABLE] ADMINISTRABLE PROGESTERONE-CONTAINING TABLETS AND METHOD FOR PREPARING THE SAME

IN THE CLAIMS

Please amend allowed claim 51 as follows. See Mark-up pursuant to 37 C.F.R. §1.121.

51. (Amended) A vaginally administrable tablet comprising micronized progesterone, a non-effervescent excipient or diluent [therefor], and an effervescent.